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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,734	11/21/2003	Solomon S. Steiner	PDT120121DIVCON	3538

23579      7590      02/07/2007  
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EXAMINER
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ALSTRUM ACEVEDO, JAMES HENRY

ART UNIT	PAPER NUMBER
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1616

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	Application No. 10/719,734	Applicant(s) STEINER ET AL.	
	Examiner James H. Alstrum-Acevedo	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 33 and 35-42 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 33 and 35-42 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>9/26/06</u> . | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

**Claims 33 and 35--42 are pending.** Applicants cancelled claim 34. Applicants have amended claims 33 and 35-38. Receipt and consideration of Applicants' new IDS (submitted 9/26/06), amended claim set, and remarks/arguments submitted on November 14, 2006 is acknowledged.

### *Moot Rejections/objections*

All rejections and/or objections of claim 34 cited in the previous office action mailed on May 17, 2006 **are moot**, because said claim has been cancelled.

### *Specification*

The objection to the abstract for being too long **is withdrawn**, per Applicants' amendments shortening the abstract to conform to the word limit guidelines in the MPEP.

### *Claim Rejections - 35 USC § 102*

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 33 and 36 under 35 U.S.C. 102(b) as being anticipated by Feldstein et al. (U.S. Patent No. 5,352,461) **is maintained** for the reasons of record set forth on page 3 of the office action mailed on May 17, 2006.

*Response to Arguments*

Applicant's arguments filed 11/14/2006 have been fully considered but they are not persuasive. Applicants' traversal of the instant rejection is based on their assertion that the disclosures of Feldstein are not anticipatory, because Feldstein does not state that the diketopiperazines encapsulating insulin are complexed to the insulin. This is found unpersuasive. The presence of both the diketopiperazine and insulin, especially when closely associated with one another, as is the case in encapsulation, would bring the two species sufficiently close for intermolecular interactions to occur that would inherently result in the complexation of insulin by the diketopiperazine. Applicants' have not provided any evidence to demonstrate that when insulin is encapsulated by a diketopiperazine that it is not inherently complexed. Applicants' citation of definitions from Wikipedia and the Hendrix Group corrosion glossary are unpersuasive because these definitions of "complex" are limited to the subfield of inorganic chemistry known as coordination chemistry. It is noted that the Wikipedia description of the term complex notes that this term, originally, "implied a reversible association of molecules and atoms through weak bonds" and that this definition has evolved as applied to the field of coordination chemistry, which is a well-developed subfield of inorganic chemistry. Therefore, the Examiner concludes that the preparation of Feldstein's diketopiperazine particles inherently includes the step of complexing the diketopiperazine and insulin, because the diketopiperazine molecules comprise several atoms having unshared electron pairs, such as nitrogen, which would interact with the encapsulated insulin to form a complex. Thus, Feldstein anticipates claims 33 and 36 and the instant rejection remains proper.

The rejection of claims 33, 35, and 37-38 under 35 U.S.C. 102(b) as being anticipated by Steiner et al. (U.S. Patent No. 5,503,852) **is maintained** for the reasons of record set forth on page 3-4 of the office action mailed on May 17, 2006.

### ***Response to Arguments***

Applicant's arguments filed 11/14/2006 have been fully considered but they are not persuasive. Applicants' traversal of the instant rejection is based on their assertion that the disclosures of Steiner are not anticipatory, because Steiner does not state that the diketopiperazines encapsulating insulin are complexed to the insulin. Similarly, as was explained above for Feldstein's disclosure, Steiner's microparticles inherently comprises an insulin/diketopiperazine complex, which forms during the process of encapsulating insulin in Steiner's diketopiperazine microparticles.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims

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2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 33 and 35-39 under 35 U.S.C. 103(a) as being unpatentable over Milstein (U.S. Patent No. 5,976,569) ("Milstein") **is maintained** for the reasons of record set forth on page 5-7 of the office action mailed on May 17, 2006.

### ***Response to Arguments***

Applicant's arguments filed 11/14/2006 have been fully considered but they are not persuasive. Applicants' traversal of the instant rejection is based on their assertion that the teachings of Milstein is not *prima facie* obvious over the cited claims of the instant application, because Milstein does not state that the diketopiperazines matrix is complexed with insulin or that the insulin is monomeric or dimeric. This is found unpersuasive. Similarly, as was explained above in the instant office action, the formation of a complex between a

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diketopiperazine and insulin is obviously a process that would occur as a consequence of the close physical association between insulin and the diketopiperazine. Thus, upon preparation of Milsteins' microparticles, insulin would be complexed with a diketopiperazine. Regarding the delivery of monomeric or dimeric insulin, it is obvious that this would be a consequence of administering Milstein's microparticles, because even if the insulin were hexameric, it would eventually form monomeric and dimeric insulin, as Applicants' have admitted on the record (see page 2, line 23 through page 3, line 2). Therefore, administration of Milstein's microparticles would obviously achieve the result of administering monomeric or dimeric insulin. For these reasons, the Examiner concludes that a person of ordinary skill in the art at the time of the instant invention would have found the cited claims *prima facie* obvious over the teachings of Milstein. The instant rejection remains proper.

The rejection of claims 40-42 under 35 U.S.C. 103(a) as being unpatentable over Milstein et al. (U.S. Patent No. 5,976,569) and further in view of Edelman, S.V. **is maintained** for the reasons of record set forth on page 7-9 of the office action mailed on May 17, 2006.

### ***Response to Arguments***

Applicant's arguments filed 11/14/2006 have been fully considered but they are not persuasive. Applicants' traversal arguments of the instant rejection are the same as those submitted to contest the rejection of claims 33 and 35-39 as being unpatentable over Milstein and that the combination with Edelman does not cure the deficiencies of Milstein. The Examiner respectfully disagrees. The Examiner's position regarding these arguments remains the same

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and is reapplied here in full. For the aforementioned reasons set forth above in the instant office action, the Examiner concludes that a person of ordinary skill in the art at the time of the instant invention would have found claims 40-42 *prima facie* obvious over the combined teachings of Milstein and Edelman. The instant rejection remains proper.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The terminal disclaimer filed on 11/14/2006 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of U.S. Patent Nos. 6,444,226 and 6,652,885 has been reviewed and is accepted. The terminal disclaimer has been recorded.



The rejections on the ground of nonstatutory obviousness-type double patenting of (1) claims 33-35 and 39 as being unpatentable over claims 11-12, 15-17, and 21-26 of U.S. Patent No. 6,444,226 (USPN '226) and (2) claims 33-35 and 40-42 as being unpatentable over claims 1-6 of U.S. Patent No. 6,652,885 (USPN '885) **are withdrawn** per Applicants submission of terminal disclaimers, which have been approved.

***Response to Arguments***

Applicant's arguments, see page 13, filed 11/14/2006, with respect to the rejections on the ground of nonstatutory obviousness-type double patenting of claims 33-35 and 39-42 as being unpatentable over the cited claims of USPN '226 and USPN '885 have been fully considered and are persuasive. The rejections on the ground of nonstatutory obviousness-type double patenting of claims 33-35 and 39-42 as being unpatentable over the cited claims of USPN '226 and USPN '885 have been withdrawn.

The rejection on the ground of nonstatutory obviousness-type double patenting of claims 33 and 35-39 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-7, and 10-14 of U.S. Patent No. 6,071,497 (USPN '497) **is maintained** for the reasons of record set forth on page 10 of the office action mailed on May 17, 2006.

*Response to Arguments*

Applicant's arguments filed 11/14/2006 have been fully considered but they are not persuasive. Applicants' traversal is based on their assertion that the claims of USPN '497 do not define microparticles wherein insulin is complexed with microparticles of a diketopiperazine. The Examiner respectfully disagrees. Applicants' arguments are the same as those discussed previously in the instant office action and the Examiner's position is the same as applied to the instant rejection. The microparticles of USPN '497 would obviously form complexes with insulin, especially since the same microparticles are being used. It is noted that the chemical structure and description thereof used to define the diketopiperazines in the original specifications of USPN '497 (i.e. col. 4, lines 1-60) and the instant application are the same. Therefore, one must conclude that the diketopiperazines will complex the insulin incorporated in the microparticles of USPN '497 in the same manner as those described by Applicants' in the instant application.

The rejection on the ground of nonstatutory obviousness-type double patenting of claims 33 and 35-39 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-7, and 10-12 of U.S. Patent No. 6,428,771 (USPN '771) **is maintained** for the reasons of record set forth on pages 10-11 of the office action mailed on May 17, 2006.

*Response to Arguments*

Applicant's arguments filed 11/14/2006 have been fully considered but they are not persuasive. Applicants' traversal is based on their assertion that the claims of USPN '771 do not define microparticles wherein insulin is complexed with microparticles of a diketopiperazine. The Examiner respectfully disagrees. Applicants' arguments are the same as those discussed previously in the instant office action and the Examiner's position is the same as applied to the instant rejection. The microparticles of USPN '771 would obviously form complexes with insulin, especially since the same microparticles are being used. It is noted that the chemical structure and description thereof used to define the diketopiperazines in the original specifications of USPN '771 (i.e. col. 4, lines 1-60) and the instant application are the same. Therefore, one must conclude that the diketopiperazines will complex the insulin incorporated in the microparticles of USPN '771 in the same manner as those described by Applicants' in the instant application.

The provisional rejections on the ground of nonstatutory obviousness-type double patenting of (1) claims 33, 35-39, and 42 as being unpatentable over claims 23-36 of copending Application No. 10/706,243 (copending '243); (2) claims 33-39 and 42 as being unpatentable over claims 1-5, 8-10, 16-17, 23-24, 26-30, and 36 of copending Application No. 11/210,710 (copending '710); and (3) claims 33-35 and 40-42 as being unpatentable over claims 1-5 and 17-23 of copending Application No. 11/329,686 (copending '686) **are maintained** for the reasons of record set forth on pages 12-15 of the office action mailed on May 17, 2006.

***Response to Arguments***

Applicant's arguments filed 11/14/2006 have been fully considered but they are not persuasive. Applicants' have not set forth any substantive arguments regarding the above cited provisional obviousness-type double patenting rejections and have requested that these rejections be held in abeyance. These rejections are maintained.

***Other Matter***

The Examiner respectfully suggests that the word "associate" on page 3, line 1 of the specification is an inadvertent error and should instead be the word "dissociate," because a hexameric species cannot "associate" to form dimers or monomers. However, a hexamer can form dimers and monomers if it "dissociates."

***Conclusion***

**Claims 33 and 35-42 are rejected. No claims are allowed.**

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

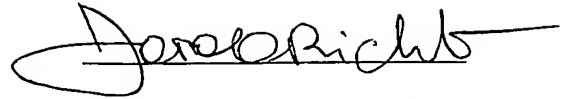
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0664. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James H. Alstrum-Acevedo, Ph.D.  
Patent Examiner  
Technology Center 1600

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A handwritten signature in black ink, appearing to read "Johann Richter", with a long horizontal flourish extending to the right.

Johann Richter, Ph. D., Esq.  
Supervisory Patent Examiner  
Technology Center 1600